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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/779,050	02/12/2001	William J. Boyle	A-570B	7999

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EXAMINER	
O HARA, EILEEN B	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 09/06/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/779,050	BOYLE ET AL.	
	Examiner	Art Unit	
	Eileen B. O'Hara	1646	

-- The MAILING DATE of this communication appears on the c ver sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 June 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) *19,20,29 and 30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18 and 21-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-30* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 1-30 are pending in the instant application.

Election/Restrictions

2. Applicant's election with traverse of Invention I in Paper No. 8 is acknowledged. The traversal is on the ground(s) that inventions I and II are related as product and process of use, and as such a search of the subject matter of invention II would substantially overlap a search of the subject matter of invention I, and therefore no undue burden is imposed by maintaining inventions I and II in a single application. This is not found persuasive because consistent with current patent practice, a serious search burden may be established by (A) separate classification thereof: (B) a separate status in the art when they are classifiable together: (C) a different field of search:. These criteria were met in the above restriction. As stated in the MPEP § 803, "a serious burden on the examiner may be *prima facie* shown if the examiner shows by appropriate explanation either separate classification, separate status in the art, or a different field of search as defined in MPEP § 808.02." Additionally, although a search of the subject matter of Invention II may substantially overlap a search of the subject matter of invention I, the methods of treatment would require substantial separate consideration for enablement, and the search and consideration of both inventions would therefore be burdensome.

The requirement is still deemed proper and is therefore made FINAL.

Claims 19, 20, 29 and 30 are withdrawn as being drawn to a non-elected invention.

Claims 1-18 and 21-28 are currently under examination.

Specification

3. The disclosure is objected to because of the following informalities:

3.1 On page 9, the legend to Figure 14 is directed to parts A and B, but in the figure there are parts A, B and C. The legend to Figure 14 should be amended to reflect what is shown in the figure.

3.2 The legend to Figure 17 on page 9 of the specification identifies the human AGP-3 receptor as SEQ ID NO: 42, which is a protein of 293 amino acids in length. However, Figure 18 is also identified as the human AGP-3 receptor, but this protein is only 291 amino acids in length.

3.3 On page 21, lines 23-24, the PCT application is incorrectly identified as WO 99/25044. The correct PCT application number is PCT/US99/25044. WO 99/25044, which is included in the IDS, encompasses a microstrip patch antenna with fractal structure.

3.4 On page 57, lines 16-18, the specification refers to the structure of the AGP-3 receptor in Figure 4, but Figure 4 consists of northern blots showing expression of AGP-3 ligand.

Appropriate correction is required.

Claim Objections

4. Claims 10-18 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 10-18 are of improper dependent form because claim 1 is directed to a composition, not a polypeptide or protein, and dependent claims 10-18 are directed to polypeptides or nucleic acids encoding such polypeptides, and as such are not further limiting.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-18 and 21-28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compositions of matter comprising the complete extracellular domain of the AGP-3 receptor protein and a vehicle, does not reasonably provide enablement for compositions of matter (including pharmaceutical compositions) that comprise portions of the extracellular domain and a vehicle. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant specification teaches that the polypeptides of SEQ ID NOS: 45 and 46 are cysteine rich domains present in the extracellular domain of the AGP-3 receptor protein (which is 165 amino acids in length) and are 37 and 38 amino acids in length, respectively (see Figures 17 and 18). The specification teaches that the full-length receptor protein has the amino acid sequence shown in SEQ ID NO: 42 (293 amino acids in length), that the AGP-3 receptor binds the ligand variously named neutrokine α, TL5, NTN-2, TNRL1 alpha, kay ligand, AGP-3 or TBAF (TNF family B cell Activation Factor), that it is primarily expressed in B cells, and that its expression correlates to increases in the number of B cells and immunoglobulins. The specification also teaches that the AGP- receptor is involved in B cell growth, survival and activation, particularly in the lymph node, spleen and Peyer's patches, and that AGP-3 transgenic

mice have higher serum globulin, increased B cell numbers and viability, decreased T cells and increased anti-nuclear and anti-dsDNA antibodies.

The claims encompass polypeptide compositions that comprise either just the polypeptide of SEQ ID NO: 45 or 46, or both, in various combinations joined to a vehicle, and also larger fragments of the extracellular domain comprising these polypeptide fragments, or replacing part or all of an antibody CDR with either one or the other or both with these polypeptides, and pharmaceutical compositions comprising such polypeptides. Because the instant specification teaches that the full-length AGP-3 receptor can bind to AGP-3, the skilled artisan would expect that the extracellular domain, which is the ligand binding domain, would bind to ligand and could be used to either purify ligand or be used in methods of therapy by binding ligand and preventing activation of the cellular receptor. The claims are enabled for the extracellular domain in such compositions or fusion proteins. However, because the claims encompass such protein derivatives that comprise only one or both of the smaller fragments of the extracellular domain (SEQ ID NOS: 45 and 46), and the specification has not provided any support or guidance that these smaller fragments could either bind the ligand or function therapeutically, the claims are not enabled for using derivatives comprising such small fragments. The instant application and the prior art have not disclosed the portion(s) of the extracellular domain required for ligand binding, and the cysteine rich domains of SEQ ID NOS: 45 and 46 are likely important in providing the correct three-dimensional spatial orientation of the extracellular domain to allow binding to the ligand, however they may not be directly involved in or sufficient for ligand binding. It would not require undue experimentation to construct such derivatives comprising the polypeptides of SEQ ID NOS: 45 and 46, however, given the fact that a

derivative comprising one of these polypeptides is only 23% of the extracellular domain, it is not predictable which species would have binding function.

Therefore, due to the lack of direction/guidance presented in the specification regarding what structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the unpredictability of determining what portions of the protein are necessary for activity and the breath of the claims, the claims are not enabled for the scope of the invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 10-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 10, 11 and 18 are indefinite because claim 1 is directed to a composition, not a polypeptide or protein, and dependent claims 10-18 are directed to polypeptides, and there is insufficient basis for these limitations in claim 1.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public u: sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1-18 and 21-28 are rejected under 35 U.S.C. 102(b) as being anticipated by Bram et al., WO 98/39361, Sept. 11, 1998, cited by Applicants.

Claims 1-18 and 21-28 are directed to compositions comprising a vehicle and various combinations of either or both the polypeptide sequences of SEQ ID NOS: 45 and 46 joined by linkers, wherein the vehicle may be an Fc region, a water soluble polymer or carbohydrate such as polyethylene glycol or dextran, polypeptides comprising an antibody sequence in which one or more amino acids from antibody variable domains or CDR regions are replaced by sequences selected from SEQ ID NOS: 45 and 46, pharmaceutical compositions comprising such polypeptides, isolated nucleic acids encoding such compositions, expression vectors and host cells. The polypeptides of SEQ ID NOS: 45 and 46 are cysteine rich domains present in the extracellular domain of the AGP-3 receptor protein (see Figures 17 and 18), the full-length receptor protein having the amino acid sequence of SEQ ID NO: 42.

Bram et al. disclose a protein identified as TACI (Transmembrane Activator and CAML-Interactor) protein (SEQ ID NO: 2), which is 100% identical to the AGP-3 receptor of the instant invention (SEQ ID NO: 42), as well as nucleic acid encoding (SEQ ID NO:1 of Bram et al.). Bram et al. teach that the TACI protein is a lymphocyte receptor protein, and identify the extracellular, transmembrane and intracellular domains, and also identify the two cysteine rich domains and teach that these domains are found in TNFR family members. On pages 7-9, Bram et al. teach that fusion proteins can be made using the extracellular domain (N-terminal fragment) or fragments thereof of the TACI protein using recombinant DNA technology, expression vectors and host cells (pages 9 and 33-41. These chimeric and fusion proteins can comprise the Fc domain of an immunoglobulin or a heavy or light chain portion of an antibody

(page 24, lines 20-30). Bram et al. also teach that such TACI polypeptide fragments may be conjugated to a carrier (page 18, lines 21-27), and that such TACI polypeptide fragments may be derivatized by the attachment of one or more chemical moieties such as polymers or sugar groups, and that such modified polypeptides may be pharmaceutically acceptable and can have therapeutic use (page 22, lines 10-34). Therapeutic uses are also described on pages 56-60.

Because claims 1-3 encompass the amino acid sequences of SEQ ID NOS: 45 and/or 46 joined by linkers, and the linkers may be the naturally occurring amino acid sequences found in the polypeptide sequence of SEQ ID NO: 42, the claims read on the extracellular domain of the AGP-3 receptor protein or fragments of the extracellular domain, joined to a vehicle, which have been disclosed in Bram et al., as described above. Therefore, Bram et al. anticipates the claims.

Conclusion

8. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eileen B. O'Hara, whose telephone number is (703) 308-3312. The examiner can normally be reached on Monday through Friday from 9:00 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached at (703) 308-6564.

Official papers Before Final filed by RightFax should be directed to (703) 872-9306.

Official papers After Final filed by RightFax should be directed to (703) 872-9307.

Official papers filed by fax should be directed to (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Eileen B. O'Hara, Ph.D.

Patent Examiner

LORRAINE SPECTOR
PRIMARY EXAMINER